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Index of Functional Changes in the Assessment Adaptive State of Comorbid Patients Treated with Trimetazidine

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Abstract: The development of myocardial ischemia and the rapid progression of atherosclerosis in patients with type 2 diabetes mellitus (DM) with the formation of diabetic autonomic cardiac neuropathy contributes to the aggravation of the prognosis of the course of cardiovascular diseases (CVD). For example, dyslipidemia with type 2 diabetes occurs in 2, and arterial hypertension is 3 times more common than without it. At the same time, it is believed that the impact of any risk factor on the level of cardiovascular mortality in diabetic patients is 3 times higher than in people without diabetes. Thus, changes in the metabolism of cardiomyocytes in ischemia can be considered as a point of application of drug effects, in particular with the help of drugs that can directly affect cellular metabolism. One of such approaches is the use of drugs from the group of so-called myocardial cytoprotectors, in particular trimetazidine. Cardiovascular diseases (CVD) are the main cause of death in patients with type 2 diabetes mellitus (DM2). In people suffering from DM2, the risk of developing CVD is 2-5 times higher than in people with normal carbohydrate metabolism. Hyperglycemia, insulin resistance and hyperinsulinemia are considered among the reasons that increase the risk of developing CVD in DM 2. Hyperglycemia is a factor that disrupts the functioning of the endothelium, which leads toincreased platelet adhesion and aggregation, increased coagulation risk factors in the bloodstream. Insulin resistance increases the synthesis of a type I inhibitor of plasminogen activators, which inhibits fibrinolytic activity of blood plasma. Trimetazidine (TMZ) is a representative of metabolic drugs. Its effect is associated with inhibition of oxidation of free fatty acids (FFA). Taking into account the violation of the metabolism of cardiomyocytes in DM and especially when combined with coronary artery disease, given the evidence of the effectiveness of TMZ in patients with stable angina, it can be assumed that the use of TMZ will be especially effective in the treatment of patients with coronary heart disease in combination with disorders of carbohydrate metabolism. Polymorbidity, impaired function of internal organs (kidneys, liver, gastrointestinal tract), age-related metabolic features affect the pharmacokinetic parameters of drugs, which reduces the effectiveness of treatment and increases the risk of adverse effects (ND) of drugs. In elderly patients, as a rule, polypragmasia occurs, sometimes as an inevitable consequence of polymorbidity. At the same time, the risk of developing ND pharmacotherapy in elderly patients is 5-7 times higher than in younger patients, and they are more severe. The incidence of ND is proportional to the number of medications taken and ranges from 10% when taking 1 drug to 100% when taking 10 medications. At the same time, it should be remembered that vitamins, phytopreparations, dietary supplements also cause the development of ND and drug interactions.

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Key words: coronary heart disease; diabetes mellitus, trimetazidine;

Introduction

In patients of older age groups, muscle mass decreases and, conversely, the amount of adipose tissue increases. This leads to an increase in the concentration of water-soluble and a decrease in the content of lipophilic drugs in the blood. In the body, the drug binds to plasma proteins, mainly albumins, and the associated part of the drug becomes inactive. Elderly patients have hypoalbuminemia, which leads to an increase in the free (unrelated) fraction of the drug in the blood and can lead to overdose and the development of toxic effects (warfarin, aspirin). Therefore, in comparison with young and middle–aged patients, the therapeutic dose of the drug is less (on average 1.5-2 times) in the elderly and elderly. The number and sensitivity of tissue receptors change with age. In particular, sensitivity to opioids, antiparkinsonian, psychotropic drugs increases. At the same time, the number of beta-adrenergic receptors decreases, their sensitivity to stimulating and blocking effects decreases, which reduces the effectiveness of the use of beta-blockers. Today, sugar diabetes (DM) and ischemic heart disease (CHD) are two sides of the same coin. Thus, the most common cause of death of patients suffering from diabetes is cardiovascular pathology: three out of four patients with diabetes die from causes associated with atherosclerosis, in most (75%) cases – from coronary heart disease. However, most patients with DM do not attach importance to their disease and do not believe that they belong to a high-risk group of cardiovascular diseases (CVD). The deterioration of prognosis for patients with coronary heart disease and DM is due to the fact that these patients often have a group of risk factors for development CVD, such as high blood pressure (BP), central obesity, dyslipidemia, renal failure, microalbuminuria. The Framingham study showed that even after adjusting the data on age, smoking, blood pressure and total cholesterol in the blood, the presence of diabetes increased the risk of developing Coronary heart disease in men by 66% and in women by 203%. Moreover, patients with DM very often have combined diseases, such as renal failure, peripheral and cerebral diseases, followed by deterioration of the prognosis of the disease. Patients with coronary heart disease and DM have certain characteristics, namely, ischemic disease develops more often at a young age. In patients with DM and CHD by 3 times
the risk of coronary vascular damage is higher, the risk of myocardial infarction is 4 times higher, while the prognosis after a heart attack is worse than in patients without DM. Due to the development of diabetic neuropathy, pain-free forms are often found in patients with DM Coronary artery disease ("mute ischemia"), therefore, stable anti-ischemic protection is especially important when choosing therapy during the day.The true number of angina episodes may be significantly higher, this is confirmed by the data of instrumental research methods. Therefore, a high risk of cardiovascular complications in patients with DM and CHD is often associated with the presence of pain-free forms of ischemia. When choosing effective antianginal and anti-ischemic therapy, it is necessary to take into account deep disturbances of metabolic processes in the myocardium in patients with DM, which are aggravated by ischemia. A decrease in the formation of adenosine triphosphate can be attributed to violations of energy processes at the tissue and cellular level and disturbances in the energy supply of the myocardium, increased oxygen demand due to its participation in the oxidation of fatty acids, resulting in a decrease in

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intracellular pH, pain, including including as a result of irritation of specific receptors in conditions of ischemia. As a result, this whole complex of interrelated processes leads to the formation of a number of reversible and irreversible changes, the progression of which ultimately leads to necrosis and death of cardiomyocytes, clinically manifested by the development of myocardial infarction. However, a doctor, using the capabilities of modern medicine, can significantly influence the development of the situation.

The aim of our study was to study the effect of cytoprotective drug – preductal OD 80 mg on the index of functional changes (IFI) in patients with type II diabetes and coronary heart disease.

Research objectives:

1. To study the clinical efficacy of preductal OD in patients with coronary heart disease and DM.
2. To identify the influence of the preduktal OD on IFI.

Materials And Methods

115 patients with coronary artery disease, stable angina pectoris III FC were under observation; in combination with Type II diabetes (59 patients). In the studied patients, a decrease in the effectiveness of antianginal therapy was noted – the reappearance of angina attacks. In 100% of patients, coronary angiography was performed, according to the results of which endovascular interventions are not required; and optimization of pharmacotherapy is advisable. The average age of the patients included in the study was 52±4.2 years. The sex composition of the patients included in the study: 100% of men, 75% of whom smoke. The diagnosis of stable angina pectoris was confirmed clinically and by the results of daily ECG monitoring, coronary angiography. In 100% of patients, stage III hypertension was noted, medically adjusted to the target values of blood pressure. The study was open, randomized. Randomization criteria: DM, cytoprotective therapy.

Thus, the first group included patients with angina pectoris – 56 people who, after assessing the homogeneity of the group, were randomized into 2 subgroups with the addition of a preductal OD to complex therapy and without the addition of a preductal OD in complex therapy. The second group – 59 people included patients with Coronary heart disease, angina pectoris and type 2 diabetes mellitus. This group was similarly divided into two subgroups, also with the addition of a preduktal OD to complex therapy and without the addition of a preduktal OD to complex therapy. The experimental group consisted of out of 30 practically healthy individuals, men. The average age of the subjects was 25.57±8.32 years. Before the start of the studies, a complete clinical and laboratory examination of volunteers was performed on the basis of Voronezh Regional Clinical Hospital No. 1. During the entire time of the research, the members of the control group led a normal lifestyle and performed their professional duties. Criteria for inclusion in the IHD group: • Men aged 25-60 years. • Presence of coronary heart disease, stable angina pectoris of functional class II. • Availability of informed consent to participate in research. Criteria for inclusion in the group of coronary heart disease in combination with type 2 diabetes: • Men, age 25-60 years. • The presence of coronary heart disease, stable angina pectoris of tension III FC. • The presence of type 2 diabetes mellitus, in the stage of subcompensation. • Availability of informed consent to participate in research. Exclusion criteria from the study: • A history of myocardial infarction less than 2 months old. before being included in the study. • Hemodynamically significant rhythm and conduction disturbances (flickering, atrial flutter, frequent extrasystole, a/b blockade of II-III degree). • Presence of large-focal postinfarction cardiosclerosis (q>0.03 s, amplitude greater than

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0.25 R). • The presence of a history of cerebral circulation disorders. • Diabetes mellitus (type I, severe course). • The presence of widespread atherosclerosis, intermittent claudication, the presence of hemodynamically significant (more 25% of the vessel diameter) narrowing of the brachiocephalic artery sections. • Chronic renal and hepatic insufficiency. • Severe diseases of the bronchopulmonary system, the presence of respiratory failure. • The presence of severe (IIB-III) circulatory insufficiency. • The presence of severe arterial hypertension • CABG.

The examination included a general blood test, a general urine test, a biochemical blood test, an ECG in 12 standard leads (the duration of QT in seconds, ST depression was calculated), EchoCG, ultrasound of internal organs, ECG – Holter monitoring. Blood pressure, height and weight were measured, and BMI was calculated. Selective coronary angiography was performed in all patients with an assessment of the number and severity of atherosclerotic lesions of the coronary arteries. All patients received standard therapy: beta-blockers bisoprolol 5-10 mg once a day or metoprolol up to 50-100 mg per day, monoiline dinitrates to prevent anginal attacks, calcium antagonists – amlodipine 5-10 mg once a day, ACE inhibitors –perindopril 5-10 mg per

day, antiplatelet agents – cardiomagnil 75 mg per day, statins – atorvastatin 20-40 mg or rosuvastatin 10-20 per day with control of total cholesterol and LDL. As a hypoglycemic therapy, patients received drugs derived from the amino acid D-phenylalaninabiguanides (metformin, glucophage) 500 mg 1-2 times a day with meals (breakfast and / or dinner) with an increase in the dose after 5-7 days to 850 mg 1-2 times in the absence of adverse events from the side Gastrointestinal tract), as well as sulfonylureas (gliclazide, diabeton MV), benzoic acid derivatives. According to the study protocol, all patients in addition to therapy CHD and type 2 diabetes, took preductal OD in a standard dosage of 80 mg 1 time a day for 3 months. Statistical analysis.

Statistical methods such as correlation analysis methods, methods for assessing the representativeness and homogeneity of the samples formed, methods for determining the reliability of averages using dependent and independent samples, methods of regression and cluster analysis, methods of variance analysis and its nonparametric analogue using the criteria of Fischer, Friedman, Kraskel-Wallis, Bonferroni, t- criteria. Charts and graphs They were performed using the built-in package of applied graphics and statistical analysis of Excel 2010 and the Statistica 8.0 package for Windows. Results and their discussion The dynamic assessment of the myocardial index (MI) in healthy and patients with coronary heart disease shows significant differences. So, if in healthy individuals during the entire follow-up period (3 visits), MI practically did not change, then in patients with coronary heart disease the picture is different. That at the first visit, MI in all patients was initially significantly higher than 17-18% (13-14.2% in the healthy group, respectively). In the group of patients with coronary heart disease without type 2 diabetes, as well as in the group of patients with coronary heart disease in combination with type 2 diabetes, an increase in MI was noted, although these changes are statistically unreliable. A completely different picture is revealed in patients when trimetazidine (preduktal OD) is included in therapy,namely: there is a statistically significant decrease in MI compared to the two previous groups at the 2nd and 3rd visits both in the group of coronary heart disease without diabetes, and to a greater extent in patients with coronary heart disease and type 2 diabetes. At the same time, the values of MI reach almost normal values, as in healthy individuals. In more detail and visually, the data on the dynamics of MI, taking into account the assessment of the non-Gaussian distribution of indicators, are shown in Fig. 3- 4 in the quarterly

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distribution. Thus, the results obtained by us on MI, most clearly manifested in patients with coronary heart disease in combination with type 2 diabetes, can characterize positive dynamics in the energy of the ischemic myocardium and can be associated with taking trimetazidine.
According to the results obtained, the myocardial index in patients with autonomic neuropathy is statistically significant it decreased at the third visit in patients who received preductal OD in complex therapy, at the same time, as in patients with or without VDKN with conventional treatment, we did not notice any changes in MI. At the first visit in patients with VDCN marked more significant figures of functional stress in contrast to patients without VDCN, who initially noted small values of adaptive potential, which may indicate a low stress of functional regulation mechanisms. During subsequent visits as part of the ongoing treatment in patients with VDKN, the values of adaptive potential are statistically significantly reduced and at the third visit they can almost reach satisfactory adaptation. In patients with VDCN who did not take preductal ONE remains high and indicates that there is no decrease in functional tension during the entire treatment time. The results obtained by us correspond to the results of similar studies.

Conclusion

The myocardial index, sharply reduced as in patients with coronary heart disease on the background of type 2 diabetes and without it, shows a significant increase in this parameter within 12 weeks when preductal OD is added to complex therapy, which may indicate the restoration of disturbed vegetative balance. According to the data of dispersion mapping, a favorable effect of the inclusion of preductal OD in the complex therapy of patients with coronary heart disease in combination with type 2 diabetes mellitus was revealed, which is associated with a partial switching of the energy mechanism of ATP synthesis from fatty acids to the glucose pathway.

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